

REMARKS

Claims 21, 23-29, 31-36, 39 and 41-45 are pending in this application. Claims 21, 23-36, 39 and 41-45 were rejected under 35 U.S.C. §112, first paragraph. Claims 21, 23-25, 27-29, 32-33, 35-36, 39 and 43-45 were variously rejected under 35 U.S.C. §102(b). Claims 21, 23-29, 31-36, 39 and 41-45 were rejected under 35 U.S.C. §103.

By this amendment, claims 32-36, 39 and 42-45 have been canceled, claims 21 and 41 have been amended and new claims 46-57 have been added without prejudice or disclaimer of any previously claimed subject matter. Support for the amendments and new claims can be found, *inter alia*, throughout the specification. Support for the amendment to claims 21 and 41 is found, *inter alia*, at page 37, lines 12-14. Support for new claims 46-48 and 52-54 is found, *inter alia*, at page 37, lines 12-14, and page 36, lines 10-11. Support for new claims 49 and 55 is found, *inter alia*, at page 28, lines 2-7. Support for new claims 50 and 56 is found, *inter alia*, at page 29, lines 22-24. Support for new claims 51 and 57 is found, *inter alia*, at pages 25-27.

The amendments are made solely to promote prosecution without prejudice or disclaimer of any previously claimed subject matter. With respect to all amendments and canceled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Applicants have carefully considered the points raised in the Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Rejection under 35 U.S.C. §112, first paragraph

Claims 21, 23-36, 39 and 41-45 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse this rejection.

Although Applicants disagree with this rejection for reasons stated in the record, the claims have herein been amended in order to facilitate disposition of the present case. The amended claims no longer contain the negative limitation regarding egg phosphatidyl glycerol or egg phospholipid.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

Rejections under 35 U.S.C. §102(b)

Claims 21, 23-25, 29, 32-33, 39 and 43-44 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Madden (U.S. Pat. No. 5,389,378). Claims 21, 23-24, 27-29, 32-33, 35-36, 39 and 43-45 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Liu (U.S. Pat. No. 5,707,608) or by Desai et al. (U.S. Pat. No. 6,074,666, herein "Desai"). Applicants respectfully traverse these rejections.

As amended herein, the claimed invention is directed to micellar compositions comprising saturated and unsaturated phospholipids and one of more hydro-monobenzo-porphyrin photosensitizer in which the micelles have an average diameter below about 100 nm.

As an initial matter, the Examiner states that the "instant claim language 'comprising' does not exclude liposomes which are also present in the prior art compositions." Office Action,

pages 4 and 5. Applicants respectfully note that the claims are directed to micelle compositions. Although the instant specification describes both liposomal and micellar compositions, and even phospholipids that may be used in both liposomes and micelles, the claimed invention is directed to a composition comprising micelles. Thus, the fact relevant to this rejection is that the cited references do not teach compositions in the form of micelles as claimed not whether or not the claimed invention excludes liposomes.

Madden

Madden describes liposome compositions but does not teach micelle compositions or production thereof. The Examiner confirms that Madden “does not explicitly disclose that the formulations contain micelles” but then asserts that “the presence of micelles in the formulations is implicit.” Office Action, page 3. Applicants respectfully disagree with this assertion. Contrary to the Examiner’s assertion on page 4 of the Office Action, Madden does not describe or otherwise use a method for preparing micelles. Madden does not describe or use the high energy processing required for the formation of micelles as taught in the present invention. In discussing preparation of the liposomal compositions, Madden teaches use of an extrusion process to generate appropriate sized liposomes “ranging from about 100 to about 120 nm in diameter.” See, for example, col. 6, lines 36-59, and col. 12, lines 27-60. As noted in the specification, the extrusion process does not produce micelles of the present invention. Thus, the method taught by Madden does not result in a micelle composition as claimed.

The Examiner further points to Wan (U.S. Pat. No. 5,329,029) and Young (U.S. Pat. No. 6,375,930) in support of the rejection over Madden. A 35 U.S.C. §102 rejection over multiple references has been held proper when the extra references are cited to: (A) prove the primary reference contains an “enabled disclosure;” (B) explain the meaning of a term used in the primary reference; or (C) show that a characteristic not disclosed in the reference is inherent. M.P.E.P.

§2131.01. Applicants respectfully submit that neither Wan nor Young provide such support to the Madden citation.

Wan makes the general statement that phospholipids are capable of forming micelles and bilayers in an aqueous medium at column 2, lines 3-5, but does not provide any teaching as to methods and conditions necessary for the production of micelles. Wan is silent with regard to formation of micelles that contain a photosensitizer as claimed and with regard to micelles of the size claimed. Nothing in Wan indicates that the compositions described in Madden inherently comprise micelles.

Young describes micelles containing texaphyrin-lipophilic molecule conjugates. Such molecules are distinct from the hydro-monobenzo-porphyrin photosensitizer and Young is silent with regard to formation of micelles that contain the photosensitizer as claimed. Nothing in Young indicates that the compositions described in Madden inherently comprise micelles.

Applicants respectfully submit that neither Wan nor Young provides any support to the teachings of Madden to demonstrate anticipation of the claimed invention by Madden.

Thus, neither the micelle composition as claimed nor the production of the micelle composition as claimed is not taught in Madden, alone or in the light of Wan or Young.

Liu or Desai

Liu describes liposome compositions and the production thereof but does not teach micelle compositions or production thereof. The Examiner acknowledges that Liu does “not explicitly disclose that the formulations contain micelles” but asserts that “the presence of micelles in the formulations is implicit.” Office Action, page 5. Applicants respectfully disagree with this assertion. Although some equipment used in Liu for the preparation of liposomes may also be used

in the preparation of micelles, Liu describes only the production of liposomes and reports only the production of liposomes in the Examples larger than 150 nm in diameter. For example, the preparation process taught in Example 5 resulted in liposome particles which averaged in size between 150 and 300 nm (col. 19, lines 5-32). In fact, Liu describes that hydro-monobenzo-porphyrin are not soluble in micellar solutions and states that such photosensitizers may be administered by using a liposome composition (col. 7, lines 32-42).

Thus, Applicants respectfully submit that, Liu teaches compositions comprising liposomes. Liu does not teach compositions comprising micelles, in particular, does not teach micelles comprising hydro-monobenzo-porphyrin, to the skilled artisan.

As in the discussion of Madden above, Applicants submit that neither the teachings of Wan nor the teachings of Young provides support to the teachings of Liu to demonstrate anticipation of the claimed invention by Liu.

As with Madden, Desai describes liposome compositions and the production thereof but does not teach micelle compositions or production thereof. The Examiner acknowledges that Desai does “not explicitly disclose that the formulations contain micelles” but asserts that “the presence of micelles in the formulations is implicit.” Office Action, page 5. Applicants respectfully disagree with this assertion. Desai does not describe or use the high energy processing required for the formation of micelles as taught in the present invention. To the skilled artisan, Desai teaches compositions comprising liposomes and not compositions comprising micelles.

Applicants also submit that neither the teachings of Wan or Young provides anything to the teachings of Desai to support this rejection.

In sum, the teachings of Madden, Liu or Desai do not explicitly or inherently anticipate the claimed invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. §102(b).

Rejections under 35 U.S.C. §103

Claims 21, 23-29, 31-36, 39 and 41-45 were rejected under 35 U.S.C. §103 as allegedly being unpatentable over Madden or Liu or Desai in view of either Lentini (U.S. Pat. No. 5,885,557) or Young in further combination with Wan. Applicants respectfully traverse this rejection.

A *prima facie* case of obviousness requires that three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20USPQ2d 1438 (Fed. Cir. 1991); MPEP §2143. If any one of these three criteria is not met, a *prima facie* case of obviousness has not been established. As presented below, Applicants respectfully submit that a *prima facie* case of obviousness has not been established.

As discussed herein, the claimed invention is directed to micellar compositions comprising saturated and unsaturated phospholipids and one of more hydro-monobenzo-porphyrin photosensitizer in which the micelles have an average diameter below about 100 nm.

The teaching of the primary references Madden, Liu and Desai and how it differs from the claimed invention is discussed above. In addition to not teaching the claimed invention, these

references provide no suggestion to modify the teaching therein to result in the claimed invention. As noted, Liu describes that the claimed photosensitizing agent is not soluble in micellar solutions.

Also as discussed above, the secondary reference Wan does not provide any teaching or suggestion as to methods and conditions necessary for the production of micelles, in particular, with regard to formation of micelles that contain a photosensitizer as claimed.

Lentini is directed to phototherapeutic treatment of the skin and mentions micelles along with liposomes and gels as formulations for use in sustained-release delivery of a photosensitizing agent, psoralen. Lentini does not teach or suggest micelles comprising saturated and unsaturated phospholipids. Further, no methods to produce micelles are taught or suggested in Lentini. Lentini does not supply what is missing from the primary references.

Thus, Lentini, in combination with any of the primary references (Madden, Liu or Desai) in further combination with Wan, does not teach or suggest the claimed invention. In addition, since none of these references teaches or suggests methods to produce micelles comprising saturated and unsaturated phospholipids and one of more hydro-monobenzo-porphyrin photosensitizer in which the micelles have an average diameter below about 100 nm, the references do not provide a reasonable expectation of success of the claimed invention. Thus, a *prima facie* case of obviousness has not been established for the cited references.

As described above, the secondary reference Young describes that texaphyrin conjugated to a lipophilic molecule can be loaded into a micelle composition. In support of this rejection, the Examiner states that “Young shows the ability of phospholipid micelles to encapsulate active agents and the primary references show the claimed porphyrins in phospholipid formulations.” Office Action, page 8. Applicants respectfully disagree with this position since the primary references do not teach or suggest a composition in which hydro-monobenzo-porphyrin is in a micelle

composition and since Young teaches micelles containing a different agent conjugated to a lipophilic molecule.

Thus, Applicants submit that Young, in combination with any of primary references (Madden, Liu or Desai) in further combination with Wan, does not teach or suggest the claimed invention. Since none of these references teaches or suggests methods to produce micelles comprising saturated and unsaturated phospholipids and one of more hydro-monobenzo-porphyrin photosensitizer in which the micelles have an average diameter below about 100 nm, the references do not provide a reasonable expectation of success of the claimed invention. Further, since Liu describes that the claimed photosensitizing agent is not soluble in micellar solutions, Applicants respectfully submit that there is no motivation in the cited references to modify the teachings therein to arrive at the claimed invention. Thus, a *prima facie* case of obviousness has not been established for the cited references.

In sum, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. §103.

CONCLUSION

Applicants believe that all issues raised in the Office action have been properly addressed in this amendment and response. Accordingly, reconsideration and allowance of the pending claims is respectfully requested. If the Examiner feels that a telephone interview would serve to facilitate resolution of any outstanding issues, the Examiner is encouraged to contact Applicants' representative at the telephone number below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 273012011300. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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